

A Most Wonderful Synthesis of 5-MeO-MiPT

Reductive Amination with NaBH₄, Acetone, and (Para)formaldehyde. Scale of 50 g

Preface

In the previous episode we synthesized 5-MeO-DMT and DMT by adding two methyl groups in succession. Starting from 5-MeO-Tryptamine we ran two cycles of formaldehyde additions. The first two to ensure the first methyl group formed at the nitrogen atom, to yield mostly 5-MeO-NMT (5-Methoxy-N-methyltryptamine). The second two to ensure the second methyl group formed at the nitrogen atom to yield 5-MeO-DMT. We ran exactly the same procedure on tryptamine to make DMT.

Looking at the structure of 5-MeO-MiPT (5-Methoxy-N-methyl-N-isopropyltryptamine) we can see that it has an asymmetric structure at the nitrogen atom. There is a methyl and an isopropyl group attached. So this time we will run an asymmetric synthesis. First run two cycles with acetone to attach the isopropyl group to yield 5-Methoxy-N-isopropyltryptamine or 5-MeO-NiPT. This might be an active substance itself, but there is little information on it. Then run two cycles with formaldehyde to attach the methyl group and yield 5-MeO-MiPT, also known as "Moxy". It works.

If we run the reaction in reverse and react with formaldehyde first, some 5-MeO-DMT might form. Owing to steric hindrance it is not possible to produce 5-MeO-DiPT with two additions of acetone anyway, so we opt to convert all of the 5-MeO-T to 5-MeO-NiPT first, and ensure that the methyl group only attaches once (no 5-MeO-DMT is formed).

Starting from tryptamine we could also make MiPT, but it seems 5-MeO-DiPT or DiPT can not be made utilizing this method simply by adding acetone in 4 cycles. "Steric hindrance", the acetone is too bulky. Possible other worthwhile substances that can be made this way is DET with acetaldehyde additions, and MET with an acetaldehyde and a formaldehyde addition.

Information on The Substance

Why make Moxy in the first place? Well I find it to be a cool substance, a bit like intelligent MDMA at 4 to 8 mg, and a sort of tryptamine version of 2c-b at the 10 mg and above dose. Warm and slow, with a positive empathogenic character. The synthesis is easy, with the same difficulty as the other reductive aminations. 5-MeO-T can be found for relatively cheap, with the other chems not difficult to find nor expensive either. And best of all it is a potent compound, so even 10 g is a lot of trips. An over-looked gem in my opinion.

Chem info:

5-Methoxytryptamine (5-MeO-T, O-Methylserotonin, mexamine) C₁₁H₁₄N₂O, Mol. weight: **190.246 g/mol**; Melting Point: **119 – 123 °C**; Slightly soluble in methanol, chloroform Appearance: white to light yellow to light orange powder.

5-MeO-MiPT (5-Methoxy-N-methyl-N-isopropyltryptamine, 3-[2-(Isopropylmethylamino)ethyl]-5-methoxyindole, Moxy) C₁₅H₂₂N₂O, Mol. weight: **246.354 g/mol**, Melting Point (HCl salt): **162 - 163 °C** (TiHKAL), (freebase): between 100 – 150 °C

Description: White to white-yellow crystals from chloroform, bitter tasting, gives a positive reaction with Van Urk test.

Solubility: Dissolves in organic solvents (chloroform, ether, benzene, acetone, etc.) when in freebase form. Dissolves in water when in the form of a salt (with HCl, H₂SO₄, etc...). Freebase is insoluble in water and salts are insoluble in organic solvents.

I found that the freebase was a pale brown or orange thick honey that would not crystallize and the HCl salt is a light tan fine powder. The HCl salt has an awful bitter taste.

Acetone (2-propanone or propan-2-one) $(\text{CH}_3)_2\text{CO}$ or $\text{C}_3\text{H}_6\text{O}$: Mol. weight: **58.08 g/mol** Boiling Point: **56.08 °C**, Melting Point: -94.9 °C, Density: **0.7845 g/ cm³** (25 °C), colorless liquid with a pungent, fruity odor. Miscible in benzene, diethyl ether, methanol, chloroform, ethanol and water

Formaldehyde (methanal) CH_2O : Mol. weight: **30.026 g/mol**, colorless gas

paraformaldehyde (CH_2O) n is formaldehyde in a polymer, in a chain of 8 – 100 units long, one must depolymerize to formaldehyde before using it, calculate molar mass like formaldehyde. White powder, or granules, mild odor of formaldehyde

formalin is an aqueous solution of formaldehyde and could be stabilized by methanol. Sold in various concentrations, 10, 20, 30%, etc. or a max of 36 - 38 % (by weight), calculate for the molar mass of formaldehyde in solution. Density: $1.08 - 1.09 \text{ g/cm}^3$

Sodium Borohydride (NaBH_4): Mol. weight: **37.83 g/mol**, white powder/ crystals, hydroscopic, forms a cake exposed to air

Acetic acid (glacial acetic acid, GAA): Mol. weight: **60.052 g/mol**, density of liquid form: 1.049 g/ cm^3 , colorless liquid

Sodium Hydroxide (lye, caustic soda, NaOH): Mol. weight: **39.9971 g/mol**, white, opaque crystals

Sodium (Na): **22.99 g/mol**, 0.9688 g/cm^3 , silvery white metallic solid

Methanol (CH_3OH , abbreviated as MeOH): boiling point: 64.7 °C, density: 0.792 g/ cm^3 , colorless liquid

Dichloromethane (CH_2Cl_2 , abbreviated as DCM): boiling point: 39.6 °C, density: 1.3266 g/ cm^3 , colorless liquid, chloroform like smell but fainter

Heptane (C_7H_{16} , n-heptane): boiling point: 98.38 °C, density: 0.6795 g/ cm^3 , colorless liquid with a faint petrolic odor

Part 1: Purification of discoloured, and impure tryptamines

The procedure is just the same like in the guide for DMT or 5-MeO-DMT:

1) Add water and a 1.02 mol eq. of GAA to the 5-MeO-T to convert the 5-MeO-T to an acetate, making sure it fully dissolves.

2) Transfer to a sep. funnel, and clean with a similar amount of DCM (or less), discard DCM, evaporate off any remaining DCM on a hotplate.

3) Add NaOH to precipitate out the freebase 5-MeO-T in water. Filter and fan dry.

After purification, should end up with a cleaner 5-MeO-Tryptamine. End up with a sparkly dry powder that weighs **46.09 g (0.242 mol)**.

Part 2: Preparation of a methanolic formaldehyde solution and the reaction in a dry ice/ acetone bath

Again pretty much the same routine.

1) 46.09 g 5-MeO-T was dissolved in 10x an amount of MeOH (fresh). Dissolve in 445 mL (could use even less).

2) Prepare the methanolic solution of formaldehyde. We will use a 2 mol. eq. for cycle 3 and at least a 2 mol. eq. for cycle 4. Probably no 5th cycle. So 4 mol. eq. from the 5-MeO-T: 0.986 mol or 29.07 g or take an excess so 30 g in 100 mL MeOH (to make a 30% sol.) Use 5 mg Na/ g CH₂O to dissolve, or 150 mg Na to dissolve 30 g CH₂O. Prepare the metallic sodium in a mineral oil bath, but toluene would have been a better choice. Use most of the Na to dissolve the CH₂O. But I realize I have been making a rookie mistake in the preparation of the methanolic solution all along.

To make a 30% sol. I need to add methanol to paraformaldehyde until the level in the beaker shows 100 mL. Pouring 100 mL MeOH onto 30 g paraformaldehyde does not make for a 30% sol.

3) pH is a high 12.1. Decide to bring to neutral with GAA. With 0.55 mL GAA bring the pH to 7.07. (Not sure if this step is necessary).

4) Prepare the TLC eluent. For the 5-MeO-T standard I mix 5 mL fresh MeOH with 3 drops of the dissolved 5-MeO-T. And for the eluent it is 10 mL ethyl acetate: 0.8 mL methanol: 0.5 mL hexane: 0.5 mL 25% ammonia. I realize later on the probably the ammonia evaporates quickly, so spots move very little. So for this TLC mix, you need to mix up the same amount before taking TLC each time (or after a period of time sitting out).

5) With dry ice and acetone, make a bath that goes to below -35 °C. This time I have a proper thermometer that reads to -50 °C and more than enough dry ice (5 kg). This is actually probably too cold for the reaction, don't really need to go below -20 °C. The temperature of the dry ice – acetone bath depends on the proportion of dry ice and acetone. Crush the dry ice before pouring on the acetone. (Wrap the dry ice in a towel and crush with a hammer).

6) Prepare a 2 mol. eq. of acetone to the 5-MeO-T for the first cycle. (0.484 mol) or 28.11 g or 35.83 mL. Start a timer for 45 min after pouring in the acetone. Not the same acetone as in the dry ice bath (use quality reagent grade stuff for the reaction). The reaction is taking place in a three-neck, 2 L round bottom flask with magnetic stirring at 500 RPM during the entire reaction.

7) Calculate the amount of NaBH₄. For the first addition will use a 1.1 mol. eq. to the 5-MeO-T, 2nd: 0.75 mol. eq. 3rd: 1.1 mol. eq. 4th: 0.75 mol. A total of 3.7 mol. eqs. or 0.8954 mol of NaBH₄ or 33.87 g.

8) For the first addition, after 45 min of the acetone mixing add 10.07 g of the NaBH₄. Before the addition, temp. is maybe -32 °C. When I add ¼ of the 10 g, temp. spikes to +5 °C. Wait some, add more dry ice and acetone to the bath, continue the additions slower when the temp. drops to -7 °C. Goes well overall. After the boro addition set a timer for 1 hour.

9) Take a TLC reading and prepare acetone addition for the second cycle. 1.5 mol eq. for the second addition or 0.363 mol or 26.87 mL. When I add acetone the second time, the temperature spikes even more severely than with the first NaBH₄ addition. So not only add the borohydride slowly, but also add the acetone slowly. Goes up to +15 °C. Add more dry ice quickly and the temperature drops quickly as well to -25 °C again.

Looking at the finished TLC, the R_x (reaction mixture) spots are not clear. Need to use a less dilute concentration of R_x .

T (5-MeO-T control) spot travelled 0.8 cm, solvent front travelled 6 cm. $R_f = 0.13$

Co (1 drop of T and one drop of R_x on top) has two spots: upper is paler with the T the same as in the T control lane. The upper spot is 2.1 cm, with the solvent front measured again to 6 cm, R_f of the upper spot is 0.35.

R_x is similar, T is very pale, upper is darker, has an R_f of 0.35 as well.

10) After the second acetone addition, set a timer for **30 min**, once that is up add the 0.75 mol. eq. of NaBH_4 or **6.87 g**. This time run a timer for **45 min**.

11) Take a TLC reading but I only do so after the first formaldehyde addition, and this was a mistake, this defeats the purpose of TLC as the 2nd TLC plate clearly shows that there was unreacted 5-MeO-T left. What I should have done is make a decision based on the TLC reading. As there was a pale 5-MeO-T spot in the R_x lane, I should have left it react for a bit more, it seems that 30 min of the acetone was not enough, maybe 1 hour would have been better. So well for trying to speed up the reaction...

12) As for the **first formaldehyde addition** or the third cycle, add a 2 mol. eq. to the 5-MeO-T amount or 0.484 mol 14.53 g or **48.44 mL**. Again, the mL amount is incorrect as I initially poured in a bit too much MeOH. And just like with the 2nd acetone addition, DO NOT pour all of the formaldehyde solution portion in at once, pour in bits, or squirt some out of a large pipette, the temp again rises too much. In a panic I add a lot of crushed dry ice, and now the temp in the bath falls *too low* to -45°C . Leave it to spin in the cold for **40 min**. I actually could have added more CH_2O maybe 70 mL of the 30% sol.

13) For the 3rd addition of NaBH_4 add a **1.1 mol eq.** to the 5-MeO-T or **10.07 g** like in the first addition. The boro does not react much when I add it, could be that the temp is a bit too low? Or steric hindrance from the isopropyl group? Leave it to spin for an **hour**.

14) Take a TLC reading for the 3rd time, but I believe it would have been best to take a new control spot before the first formaldehyde and 3rd boro additions. This is not like a DMT synth where there might be a mixture of NMT and DMT quite early on, here we need to make 5-MeO-NiPT first. So maybe I should have taken a 5-MeO-NiPT "T" spot by using a long pipette and dissolving 3 drops in 5 mL fresh MeOH. Then after these additions take a TLC reading as if it were a new reaction to see how 5-MeO-NiPT disappears as it reacts.

Well the spots move very little, they are very low and the R_f is small. (should have prepared fresh eluent). T lane has an R_f of 0.034, small lower spot.

Co is two spots, lower same as T, upper a larger streak. Maybe 0.102 R_f .

R_x is same as Co except upper spot is much larger, lower is very faint.

15) Add about **40 mL CH_2O** (bit less than 2 mol. eq. to the 5-MeO-T amount) and leave it to spin for **30 min**. As I recall, the temp does not rise.

16) Wait about 20 min more and add another 5 g NaBH_4 . Temp does not rise. Leave overnight and in the morning I take the last TLC plate. It looks promising: only one faint upper spot.

Part 3: Work-up Of The Reaction, Things Get Messy

I opt to follow the exact same procedure as with the DMT work-up. The first step is to get rid of most of the MeOH.

1) Transfer the reaction mixture to a 2 L one-neck round bottom flask, and use **vacuum distillation** in an attempt to boil off the MeOH at close to room temp. Does not go well, there is some sort of leak in the system, and my pump is not up to snuff for this type of job, goes very slowly and temps eventually rise above a satisfactory level. Distill off about 200 mL of the MeOH which I pour back into the MeOH barrel.

2) Add 300 mL dH₂O to the reaction mixture and solids appear!

3) After a total addition of **350 mL dH₂O** an oil appears as well and white solids which dissolve back? Decide to check the pH and it is a high 12.12.

4) Transfer to a 2 L sep. funnel and extract with DCM. For the first extract use 150 mL DCM for the first extract, 100 mL DCM for the second, and 75 mL for the third. Notice that most of the goods were extracted the first time around.

5) Believe I extracted with 330 mL DCM in total but in the beaker the level shows up to 510 mL. Maybe a tonne a product.

6) Pour the aq. layer into a separate beaker, have just over 600 mL. (end up discarding later)

7) Dry the DCM layer with MgSO₄. I will take 350 mL as the DCM amount. At 25 °C 1.76 g H₂O dissolves in 100 g DCM, so need to remove ~ 6.16 g H₂O. Let us approximate the absorption of MgSO₄ as 0.5g H₂O / g. So need ~ 12 g MgSO₄. In a beaker with magnetic stirring pour in the magnesium sulfate and notice that the DCM clears up, but as well the MgSO₄ captures quite a bit of the product. Should have used less than 12 g.

8) Pour the dry DCM layer through a large medium speed fan flute folded qualitative filter paper into a pyrex dish set on top of hotplate. Does this in a fumehood. Did not attempt vacuum distillation, as I know I will have poor luck until I get a better pump.

9) Transfer the sticky viscous brown-golden honey like oil to a 250 mL beaker. Beforehand I had weighed the beaker: 94.53 g. Weight is 62.46 g and reason that this is too much. A 100% yield of 5-MeO-MiPT would weigh 59.62 g. Decide to leave the plate to evaporate some more as there is a DCM smell that lingers. Overnight, most if not all of the DCM has evaporated, and the weight now is a much more reasonable **50.75 g**. Will see and try if I can use a hot heptane extraction just as I did with the DMT to leave impurities behind.

10) Begin by heating to boiling about 1 L heptane in a beaker set on a spare heating mantle, on a separate hotplate + magnetic stirrer the brown – red honey is spinning at 70 °C. Start doing 100 mL boiling extracts with the heptane. Decant each time into a pyrex dish, the heptane goes cloudy as it cools. Make sure to not pour any of the bottom layer in. The going is slow, the heptane picks up much much less of the product each time, lose track of how many times I extract, go mostly 75 mL fresh heptane each time. Unsure of how much heptane I use, could be a bit over **1.5 L heptane** until finally only sludge or mostly sludge is left. Might have even extracted more product but I got tired. The sludge which I discard weighs 10.33 g, so I should have about 40.42 g product.

The hot heptane method was ideal for DMT and 5-MeO-DMT, much more product was picked up each time, especially so for DMT, it was not difficult at all to extract. With 5-MeO-MiPT I would pick another method or skip it all together and possibly attempt to vacuum distill the amine to get a clean product. Even more so as from the heptane you will still not end up with a crystalline product, just more honey, albeit clean.

11) As the heptane cools, it remains cloudy. If it looks clear, blowing it just a bit makes the heptane cloudy. There is a layer on the bottom of the plate with most of the product, but the heptane still holds a lot. So I place the plate into a freezer checking often to see if the layer goes clear. Takes a long time, the layer only clears up in the morning after sitting overnight.

12) Decant the cold heptane but spill a bunch as the plate is so full. Leave the plate to fully dry and in the meantime distill the heptane. Use a 2 L RBF that is rather full. Heptane distills very easily and even with simple distillation bumping occurs when the distillation starts. Set a magnet to stir quickly when the first very large bubbles appear. When distilling I do not collect the first 50 or so mL, collect about 1.4 L which I return to my heptane barrel. The very last portion I leave to evaporate in a crystallizing dish. There is product in there!

13) The product in the main plate remains a honey like liquid. Very sticky, a pain to deal with it. It refuses to crystallize, I knead it a bit, and leave it for longer. No crystals appear seem to appear. What I could have tried was to transfer to a beaker and stir violently with a spoon, the goo would have picked up thousands of small air bubbles, it would have started to appear opaque, it would have gotten harder and harder to stir, until rather suddenly it would turn white and freeze up. Didn't try this. Just a fantasy. However, in the small crystallizing dish with the distilled product, some crystals do appear, but I end up transferring everything to the main plate.

14) Try freezing the plate. This doesn't change anything. It remains an ivory pale brown – orange oil, sticky honey. Cannot think of anything else, this product is too sticky to handle. I'm tellin you, this could turn Winnie the Pooh into a bad bwoy! Woah Jungle man!

15) Decide to make the **HCl salt form**. If I have 40 g of this stuff which I presume to be 5-MeO-MiPT freebase, this makes for 0.162 mol. If using 36% HCl, 1L contains 11.64 mol, so need 0.0139 L or **13.9 mL of concentrated aq. HCl**. Dilute this in 70 mL **isopropyl alcohol (IPA)**.

16) First dissolve the mass in 100 mL IPA, takes some stirring but it eventually fully dissolves in the IPA, makes for a pretty golden solution.

17) Add over half of the HCl in IPA, and everything goes well, there is no colour change, but the pH drops to below 8. And I continue adding too liberally, in too large of portions of portions, too quickly. Once below pH 7 the smallest addition makes for a rapid drop, as there is less freebase left. Totally overshoot. Always, always when doing this type of acidification/ salting procedure; LEAVE SOME FREEBASE out. If you overshoot you can pour freebase back in to neutralize. Don't be stupid and do all at once.

I was a fool for forgetting this, the pH drops to 2.25 and there was some darkening in colour at one point which I ignored. This is when the HCl product appeared. Do not use all of the HCl, so will not be 40 g. In a best case scenario you would lower the pH to 2-3 below the pKa of the freebase, in this case would guess it is similar to DMT or 5-MeO-DMT, so a pKa of about 9. A target pH of 6, 6.5 is sufficient.

18) Evaporate on a hotplate with a fan blowing the IPA + water, it takes some time to fully evaporate and there might be some smell left.

19) The product still remains a sticky liquid. Even more a liquid than the freebase. Hmm, no good! In frustration I transfer to a beaker.

20) Pick up a Hazelwood spoon and I churn up the butter just like ol' ma used to. Remember folks, if you have the milk, you gotta churn up some butter. Beat the son of a gun.

21) Air bubbles form and what I was fantasizing about with the freebase actually occurs. The air bubbles seem to help crystals form, or maybe the agitation helps to drive out more IPA? It becomes harder and harder to churn. Soon a white solid forms, but it is still damp with some water and IPA. Still very sticky, that sticky son a bitch.

22) Pour in about 100 mL ice-cold ethyl acetate to help dislodge it from the beaker. Get most of it out onto filter paper over a Büchner funnel. I'm about to drown the fucker in freezing EtOAC. Life is not going well, some of the shit is left stuck to the beaker, but just too pissed to get every single hopeless morsel off.

23) Attempt to clean with EtOAC, but what good does it do? I need a more powdery form than some big ass temple ball.

24) Fan dry but now but the EtOAC is hard to get out. Blend it with a few beans of Hamesho Kebena. Need to buy a mortar and pestle one day, seems like folks can't enjoy a fine cup of Joe anymore without tripping balls.

25) Eventually weigh the mostly fine powder which stays a light tan even with repeated washings. Have about **31.5 g or 0.111 mol**. From the starting 46.09 g of 5-MeO-T, this represents a **46% yield**.

26) With a two-neck Thiele tube attempt to take an accurate melting point. First attempt is not so good, not enough product, couldn't really see what was up, might also have been still damp with ethyl acetate. Much later on, take a fairly good reading, but I miss the exact point when it really started to melt. It sinters or maybe forms some sort of a gel starting at 120 °C, more gelling occurs at 140 °C, and maybe at 145 °C it really melts. Would say the melting point of the HCl salt is **144 – 146 °C**. This is below that of TiHKAL. Plan to send it out for testing in the near future.

Afterword, and a call to prayer

What a great little substance, I really do like this one, but it could be not to everyone's liking. What for some is a pleasant bodyload, for others unpleasant. A warm stoning effect, for others a heavy head, and less thoughts than on other psychedelics.

An interesting one, potent, and not difficult to synthesize. Enjoy.

Analysis and Commentary

The product was tested with HPLC and it turned out to be not so pure. It was tested to be **79.1 % 5-MeO-MiPT HCl**, with the rest a mixture of unreacted 5-MeO-Tryptamine, and some 5-MeO-NMT. Of the remaining 20%, 13 – 16% was 5-MeO-Tryptamine. Just as TLC showed after the second cycle, not all of the substrate reacted. Most certainly the acetone cycles were too short.

The reactant carried over to the formaldehyde cycles, and it seems that only 5-MeO-NMT managed to form. So two cycles are not enough for any 5-MeO-DMT to form, but other parameters doubtless had their effects as well.

The impurity of the final product most likely hindered formation of a solid form of freebase 5-MeO-MiPT. It also would have lowered the melting point of the mixture. So it could be that Shulgin's melting point is correct.

The final product is fine for me, just maybe need to dose a few extra mg. I would assume the 5-MeO-NMT is minimally active, and at these amounts harmless and inactive.

Why such a molar excess of acetone or formaldehyde in these reactions? Well, it does seem that conditions do warrant such amounts. I don't have an exact explanation, but TLC seems to show that these excesses are needed. Maybe it just doesn't manage to react so easily, the answer might be in the original thread in the Russian Hyperlab forum...

Try it guys, and remember to look as the reaction goes along on TLC.

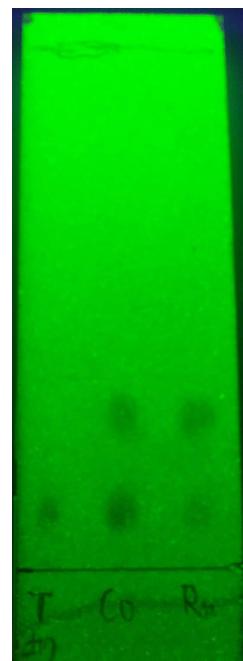
Overall, the Moxy is a mixed bag. Sometimes it works well, while other times it doesn't seem as positive or strong. You need to notice the effects more, those who frequently use substances might write it off as a weak compound. But it has its place. But in the end I do not think it is in the league of the classics: LSD, mescaline, or shrooms.

Peace Out

A few pictures, didn't take many this time, TLC Nr. 4 is missing



TLC Plate Nr. 1



TLC Plate Nr. 2



TLC Plate Nr. 3



Plate with the freebase oil after heptane poured off, evaporated



Final HCl product